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| EXAMINER |
|---|
| YAEN, CHRISTOPHER H |

| ART UNIT | PAPER NUMBER |
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| 1642 | 8 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/889,300 | Applicant(s) ECKERT ET AL. | |
|---|---|---|---|
| | Examiner Christopher H Yaen | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. In regards to claim 5, in the recitation of the phrase *"fine specificity"*, it is unclear as to what type and degree of specificity is required for the antibody. Clarification is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single epitope recognized by mAB HE2, does not reasonably provide enablement for antibodies which are directed to different epitopes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 6 is directed to pharmaceutical compositions for vaccination against cancer comprising an antibody directed against EpCam, wherein the antibody is directed against different epitopes of membrane antigen. The instant specification

details and discloses the use of HE2, a monoclonal antibody directed against EpCam, but is silent with regard to using antibodies directed against different epitopes. Because there is a lack of disclosure concerning the further limitation, the instant application invites the skilled artisan to experiment.

The factors which must be considered in determining undue experimentation are set forth in *In re Wands* 8 USPQ2d 1400. The factors include: (1) quantity of experimentation, (2) the amount of guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the predictability of the art, and (7) breadth of the claims.

With regards to factors one and two cited above, the quantity of experimentation required to determine which antibodies are able to bind to the different epitopes, there is insufficient guidance in the written description for accomplishing and determining such.

With regards to factors four, five, and six, it is noted that there is a great deal of unpredictability associate with determining which antibodies are reactive to an antigen as it is well known in the art, that screening and panning techniques are used to determine which antibodies are reactive to a specific antigen. The instant specification has not indicated which other antibodies will be used in the pharmaceutical composition, and hence it would require a great deal of experimentation to determine which antibodies are useful and are able to react to the membrane antigen.

With regard to factors three and seven cited above, it is noted that the working examples are limited to *in vivo* and *in vitro* examples using a single antibody, namely mAB HE2. The instant application is silent with regard to using multiple antibodies with

reactivities to multiple or different epitopes of a membrane antigen. Such is not seen as sufficient to support the breadth of the claims, wherein the scope of the claims encompasses multiple antibodies with different epitope reactivities.

6. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 and dependent claims thereof are drawn to a pharmaceutical compositions for the vaccination against cancer comprising antibody(ies) against EpCam. Currently as interpreted, the claims are drawn to a product for vaccination, wherein the vaccination is interpreted to mean a prophylactic compound for the prevention of cancer. The instant specification is silent with regards to using this composition in this manner. Because the instant specification has insufficiently disclosed this subject matter, it invites the skilled artisan to experiment.

With regards to factors one and two cited above, the quantity of experimentation required to prevent cancer, through vaccination using an antibody directed against EpCam, is high, because as evidenced by (Evans *et al.* Q J Med 1999; 92:299-307), it has been shown that an cancer vaccine can only, at best, be used as a therapeutic, and not as a prophylactic (see pg 303 column 2). It is noted that the instant specification is silent in this regard, and is thus seen as insufficient and inadequate guidance in the written description for accomplishing such.

With regard to factors four, five and six cited above, it is noted that the there is a great deal of uncertainty and unpredictability associated with vaccination against cancer (Evans *et al.*). The prior art teaches that vaccines against cancer are difficult and as stated above, can be, only at best, used as therapeutics and not as prophylactics (Evans *et al.*). It is difficult to determine which patients will develop cancer and therefore hard to determine which ones to administer this composition.

With regards to factors three and seven cited above, it is noted that the working examples as stated above (see paragraph 6 of this office action), are only directed to using the pharmaceutical composition as a therapeutic. There is virtually no mention of using such composition as a prophylactic. Such is not seen as sufficient to support the breadth of the claims, wherein the scope of the claims encompasses vaccination in general.

In the above cited rejections (paragraph 6 and 7), it is noted that Law requires that the disclosure of an application shall inform those skilled in the art ho to use applicant's alleged discovery, not how to find out how to use it for themselves., see *In re Gardner et al.* 166 USPQ 138 (CCPA 1970).

***Claim Rejections - 35 USC § 102***

7. The following rejection is based on the interpretation that the term *"vaccination"*, is meant to be interpreted as a therapeutic. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Braun *et al.* (Clinical Cancer Research 1999 Dec; 5:3999-4004). Claims 1-3 are drawn to a pharmaceutical composition for the vaccination against cancer comprising at least one antibody that is directed against Ep-CAM, is of animal origin and is a monoclonal antibody. Braun *et al.* disclose of a monoclonal antibody developed in a mouse that is specific for Ep-CAM, and Braun *et al.* further disclose of using this antibody for the elimination of tumors in patients by intravenous infusion of 500 mg of the antibody (see abstract).

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Braun *et al.* in view of Pardoll D (Immunology Today 1993;14(6):310-316). Claim 7 is drawn to a pharmaceutical composition for vaccination against cancer comprising at leat one antibody directed against Ep-Cam, further comprising at least one adjuvant. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Braun *et al.* as previously discussed above, does not specifically disclose of using an adjuvant in combination with an antibody to administer compound. Pardoll D does however, disclose of using adjuvants in combination with vaccines for the treatment of cancer.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to develop a compound for treating cancer comprising an antibody against Ep-Cam and an adjuvant, because the prior art provides sufficient motivation to practice the invention as claimed. The suggestion/motivation for doing what the applicant has claimed is that is was already known in the art that an antibody against EP-Cam was in existence and that is was also being used as a form of treatment in

cancer (Braun *et al.*). It was also well known in the art that adjuvants combined with antibodies could increase immunogenicity of a compound being administered. Therefore, it would have been *prima facie* obvious at the time of the invention to derive of a compound made up of an antibody against Ep-Cam and an adjuvant because both independently were well known in the art. One would have been motivated to combine the two references to arrive at the claimed invention because each product independently work well, and to combine the two products would only improve the combined products. Therefore the invention as claimed is obvious.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
May 2, 2002

ANTHONY C. CAPUA
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